10/043,268

(FILE 'HOME' ENTERED AT 12:39:27 ON 01 JUN 2004)

FILE 'REGISTRY' ENTERED AT 12:39:45 ON 01 JUN 2004
L1 STRUCTURE UPLOADED

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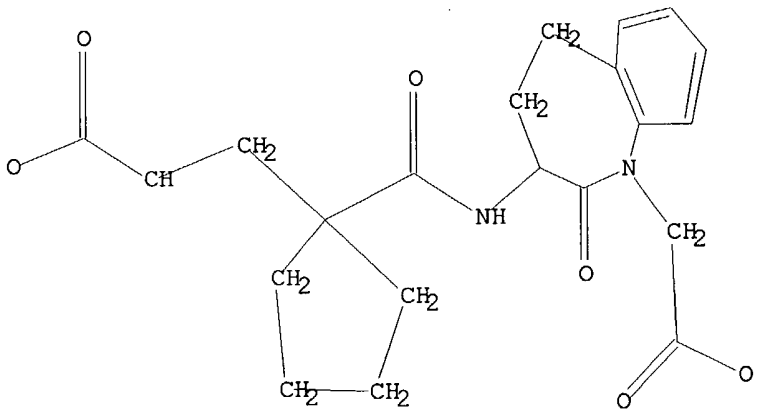
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 12:40:11 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 3 TO ITERATE

100.0% PROCESSED 3 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 3 TO 163
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 12:40:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 78 TO ITERATE

100.0% PROCESSED 78 ITERATIONS 60 ANSWERS
SEARCH TIME: 00.00.01

L3 60 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY 155.42 TOTAL SESSION 155.63

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 12:40:22 ON 01 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 1 Jun 2004 VOL 140 ISS 23
FILE LAST UPDATED: 31 May 2004 (20040531/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l3
L4 8 L3

=> d 1-8 bib abs

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:660247 CAPLUS
DN 139:169370
TI Immediate-release pharmaceutical formulation with enhanced bioavailability
IN Gorissen, Henricus R. M.
PA Solvay Pharmaceuticals B.V., Neth.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003068266	A1	20030821	WO 2003-EP50014	20030211
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1336414	A1	20030820	EP 2002-75623	20020214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	EP 2002-75623	A	20020214		

OS MARPAT 139:169370
AB The present invention relates to an immediate release formulation with enhanced bio-availability comprising a solid homogeneous and thermostable solution of a poorly water-soluble biol. active substance, characterized in that the solid solution comprises: (a) the active substance in an amount of between 10 and 50% of the total weight of the formulation, (b) a nonionic hydrophilic surfactant ingredient, which is in the liquid form between 15° and 30°C, in an amount of between 20% and 70 % of the total weight of the formulation and (c) a pharmaceutically acceptable organic polymer or mixture of

polymers, which polymer or mixture of polymers is in a liquid form above 60°C and in a solid form below 30°C, in an amount of between 5% and 70% of the total weight of the formulation, and (d) optionally comprises a disintegrating agent in an amount of between 1% and 10% of the total weight of the formulation. The invention further relates to active substances formulated into the above form and methods for producing the formulation. For example, capsules containing 3-[[[1-[(2R)-2-(ethoxycarbonyl)-4-phenylbutyl]cyclopentyl]carbonyl]amino]-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid Ca salt 103.7, Tween 80 311, and PEG-6000 234 mg per each, were formulated.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:571009 CAPLUS
DN 139:138736
TI Solid benzazepine salts preparation for pharmaceuticals
IN Van Der Eerden, Joris A.; De Jong, Paulus P. g.; Van Der Meij, Paulus F. C.
PA Solvay Pharmaceuticals B.V., Neth.
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003059939	A1	20030724	WO 2003-EP515	20030115

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2002-75621 A 20020116
NL 2002-1019762 A 20020117
OS MARPAT 139:138736
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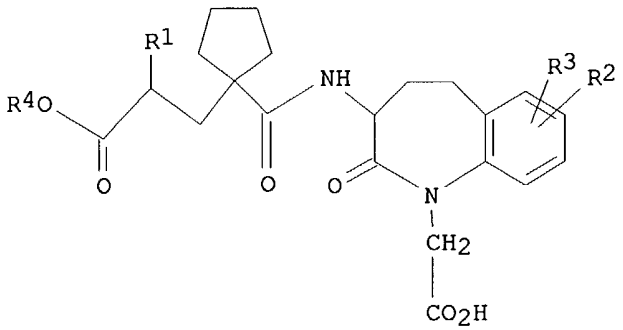

I

AB The present invention relates to benzazepine salts and bivalent metal ion salts such as magnesium, calcium and zinc salts. Also pharmaceutical

compns. comprising the salts can be used in the treatment of hart disorders or hypertension, in the improvement of gastrointestinal blood flow or in the treatment and prophylaxis of cardiac damages induced by adriamycin and comparable anti-cancer drugs. Salts of I prepared include, Ca, Mg, Zn, Li, K, and Na and the S-α-methylbenzylamine salt which is useful as an intermediate in the production of the above mentioned salts.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:363526 CAPLUS
DN 139:94628
TI SLV-306 Solvay
AU Tabrizchi, Reza
CS Faculty of Medicine Basic Medical Sciences Health Sciences Centre, Memorial University of Newfoundland, St John's, NF, A1B 3V6, Can.
SO Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(3), 329-332
CODEN: COIDAZ; ISSN: 1472-4472
PB Thomson Current Drugs
DT Journal; General Review
LA English
AB A review. SLV-306 is an orally active mixed neutral endopeptidase/endothelin converting enzyme inhibitor under development by Solvay SA for the potential treatment of essential hypertension and congestive heart failure. The compound is currently undergoing phase II clin. trials in Belgium.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:304371 CAPLUS
DN 138:49186
TI SLV-306
AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2002), 27(1), 27-31
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. The synthesis, pharmacol. actions, and clin. studies of SLV-306, a new drug for treating hypertension, is described. SLV-306 is synthesized by acylation of 3(S)-amino-2-oxo-2,3,4,5-tetrahydro-1H-1-benzazepine-1-acetic acid tert-Bu ester with 1-[2-(R)-(ethoxycarbony)-4-phenyl-butyl]cyclopentanecarboxylic acid by methanesulfonyl chloride and triethylamine in dichloromethane to yield the amide (III), which is then treated with trifluoroacetic acid to eliminate the tert Bu ester group.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:50486 CAPLUS
DN 134:105881
TI Pharmaceuticals with protective effects against oxidative-toxic substances, particularly against cardiotoxic substances
IN Rozsa, Zsuzsanna; Papp, Julius G.; Thormahlen, Dirk; Waldeck, Harald
PA Solvay Pharmaceuticals G.m.b.H., Germany
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001003699	A1	20010118	WO 2000-EP6525	20000710
	W: AU, BR, CA, CN, CZ, DZ, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RU, SK, TR, UA, US, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19932555	A1	20010118	DE 1999-19932555	19990713
	BR 2000012442	A	20020402	BR 2000-12442	20000710
	EP 1200095	A1	20020502	EP 2000-947960	20000710
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	TR 200200053	T2	20020521	TR 2002-20020005320000710	
	JP 2003504336	T2	20030204	JP 2001-508979	20000710
	NO 2002000132	A	20020312	NO 2002-132	20020111
	ZA 2002000265	A	20030113	ZA 2002-265	20020111
	US 2003040512	A1	20030227	US 2002-43268	20020114
PRAI	DE 1999-19932555	A	19990713		
	WO 2000-EP6525	W	20000710		

OS MARPAT 134:105881

AB The invention relates to the utilization of benzazepine-N-acetic acid derivs. which contain an oxo group in addition to the nitrogen atom in the α-position and which are substituted in the third position by a 1-(carboxyalkyl)cyclopentylcarbonylamino group and to their salts and biolabile esters for the prophylaxis and/or treatment of heart damages caused by cardiotoxic doses of drugs or chems. in large mammals and particularly humans. beings. The invention particularly relates to the prophylaxis and/or treatment of heart damages, especially myocardial damages, which may occur during cytostatic chemotherapy. The invention further relates to the utilization of these benzazepine-N-acetic acid derivs. for adjuvant treatment in therapy in which drugs, which have undesirable oxidative-toxic side effects, are used. The invention addnl. relates to the production of drugs suitable for the prophylaxis and/or treatment or adjuvant treatment. Thus, tablets were prepared from (3S,2'R)-3-(1-[2'-(ethoxycarbonyl)-4'-phenylbutyl]cyclopentane-1-carbonylamino)-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetic acid 20, corn starch 60, lactose 135, and gelatin (10% solution) 6 mg/tablet.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:574119 CAPLUS
DN 133:172184
TI Medicament for treatment of high blood pressure
IN Wilkins, Martin R.; Thormaehlen, Dirk; Waldeck, Harald
PA Solvay Pharmaceuticals G.m.b.H., Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19906310	A1	20000817	DE 1999-19906310	19990216
	WO 2000048601	A1	20000824	WO 2000-EP1068	20000210
	W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RU, SK, TR, UA, US, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	NZ 514058	A	20010928	NZ 2000-514058	20000210
	BR 2000008260	A	20011106	BR 2000-8260	20000210

	EP 1154777	A1	20011121	EP 2000-903681	20000210
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	TR 200102386	T2	20020121	TR 2001-20010238	20000210
	JP 2002537258	T2	20021105	JP 2000-599393	20000210
	ZA 2001005828	A	20020715	ZA 2001-5828	20010716
	NO 2001003958	A	20011015	NO 2001-3958	20010815
	US 2002052361	A1	20020502	US 2001-930186	20010816
	US 6482820	B2	20021119		
PRAI	DE 1999-19906310	A	19990216		
	WO 2000-EP1068	W	20000210		

OS MARPAT 133:172184

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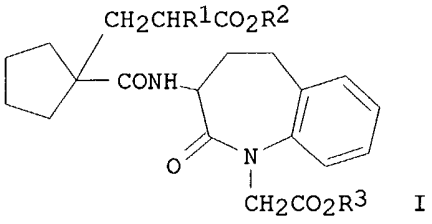

I

AB Benzazepine-N-acetic acid derivs. I [R1 = (substituted) phenylalkyl, naphthylalkyl; R2, R3 = H, biolabile ester-forming group] are useful for treatment of high blood pressure regardless of etiol., especially certain forms of secondary hypertension associated with noncardiac disorders. Thus, rats with hypoxia-induced pulmonary hypertension, treated with (3S,2'R)-3-[1-(2-carboxy-4-phenylbutyl)cyclopentane-1-carbonylamino]-2,3,4,5-tetrahydro-2-oxo-(1H)-1-benzazepine-1-acetic acid (II) (40 mg/kg i.p./day by osmotic minipump), showed a reduction in pulmonary arterial pressure with no effect on the systemic blood pressure. A sterile injection solution contained II 10, Na2HPO4.7H2O 43.24, NaH2PO4.2H2O 7.72, NaCl 30.0, and H2O 4948.0 mg.

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:196303 CAPLUS
DN 128:239479
TI Benzazepineacetic acid derivatives promoting gastrointestinal blood circulation
IN Rozsa, Susanna; Papp, Julius Gy.; Thormaehlen, Dirk; Waldeck, Harald
PA Solvay Pharmaceuticals G.m.b.H., Germany
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19638020	A1	19980319	DE 1996-19638020	19960918
	EP 830863	A1	19980325	EP 1997-115603	19970909
	EP 830863	B1	20000510		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	ES 2145545	T3	20000701	ES 1997-115603	19970909
	US 5783573	A	19980721	US 1997-929114	19970915
	JP 10101565	A2	19980421	JP 1997-251928	19970917

PRAI DE 1996-19638020 A 19960918
OS MARPAT 128:239479
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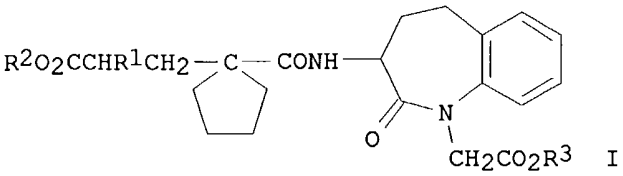

I

AB Benzazepineacetic acid derivs. I [R1 = (substituted) phenylalkyl, naphthylalkyl; R2, R3 = H, group forming a biol. labile ester] and their salts are useful in pharmaceutical compns. for treatment and/or prophylaxis of disorders in the gastrointestinal (mesenteric) circulation of various etiol. in humans and large mammals. Thus, in rats with streptozotocin-induced diabetes, the mesenteric arterial blood pressure was 9 mL/min; this was increased to 14 mL/min by treatment with I (substituents not specified) at 30 mg/kg/day orally for 8 wk. Tablets were prepared containing (3S,2R)-I (R1 = PhCH2CH2, R2 = Et, R3 = H) (II) 20, corn starch 60, lactose 135, and gelatin 6 mg. II was prepared from di-Et malonate and phenethyl bromide via 2-carboxy-4-phenylbutyric acid and Et α-(2-phenethyl)acrylate, reaction with cyclopentanecarboxylic acid, resolution with L(-)-α-methylbenzylamine, condensation with tert-Bu 3-amino-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetate, etc.

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:646474 CAPLUS
DN 125:301029
TI Preparation of 3-[[(1-carboxyalkyl)cyclopentyl]carbonylamino]benzazepin-1-acetates and analogs as neutral endopeptidase inhibitors
IN Waldeck, Harald; Hoeltje, Dagmar; Messinger, Josef; Antel, Jochen; Wurl, Michael; Thormaehlen, Dirk
PA Kali-Chemie Pharma Gmbh, Germany
SO Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 733642	A1	19960925	EP 1996-104265	19960318
	EP 733642	B1	20001129		
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	ZA 9601243	A	19960827	ZA 1996-1243	19960216
	IL 117265	A1	20000716	IL 1996-117265	19960226
	SK 281079	B6	20001107	SK 1996-354	19960315
	AT 197801	E	20001215	AT 1996-104265	19960318
	ES 2152444	T3	20010201	ES 1996-104265	19960318
	PT 733642	T	20010330	PT 1996-104265	19960318
	CN 1147506	A	19970416	CN 1996-104257	19960320
	CN 1059436	B	20001213		
	RU 2159768	C2	20001127	RU 1996-105383	19960320
	CA 2172354	AA	19960924	CA 1996-2172354	19960321
	CA 2172354	C	20021008		
	AU 9648210	A1	19961003	AU 1996-48210	19960321
	AU 701271	B2	19990121		
	NO 9601181	A	19960924	NO 1996-1181	19960322

	JP 08269011	A2	19961015	JP 1996-66703	19960322
	US 5677297	A	19971014	US 1996-620213	19960322
	CZ 289245	B6	20011212	CZ 1996-863	19960322
	PL 184336	B1	20021031	PL 1996-313433	19960322
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PRAI	DE 1995-19510566	A	19950323		
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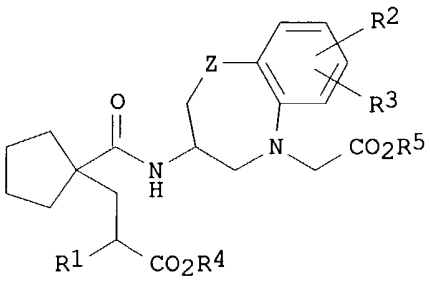

I

AB Title compds. (I; R1 = alkoxyalkoxyalkyl, phenylalkyl, phenoxyalkyl, etc.; R2,R3 = H or halo; R4,R5 = H, metabolism labile ester residue; Z = CH2, O, S) were prepared Thus, tert-Bu 3-amino-2,3,4,5-tetrahydro-2-oxo-1H-1-benzazepine-1-acetate was amidated by 1-(2-ethoxycarbonyl-4-phenylbutyl)cyclopentanecarboxylic acid (preparation each given) to give I (R1 = CH2CH2Ph, R2 = R3 = H, R4 = Et, R5 = CMe3, Z = CH2). Data for in vitro and in vivo biol. activity of I were given.

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FILE 'REGISTRY' ENTERED AT 16:05:04 ON 01 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 31 MAY 2004 HIGHEST RN 688001-12-9
DICTIONARY FILE UPDATES: 31 MAY 2004 HIGHEST RN 688001-12-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s zorubicin/cn
L2 1 ZORUBICIN/CN

=> d rn

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 54083-22-6 REGISTRY

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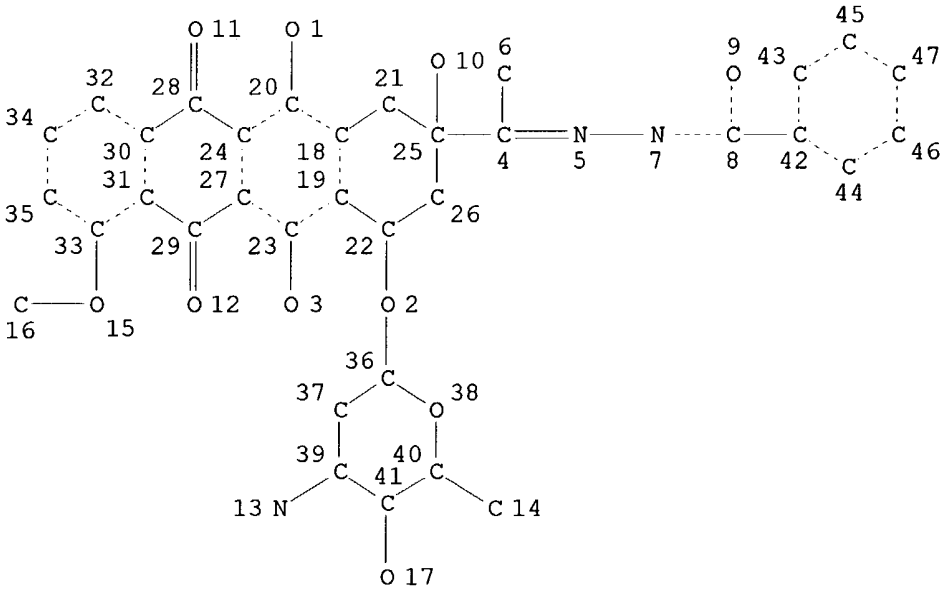

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L4            1 DOXORUBICIN/CN

=> d rn

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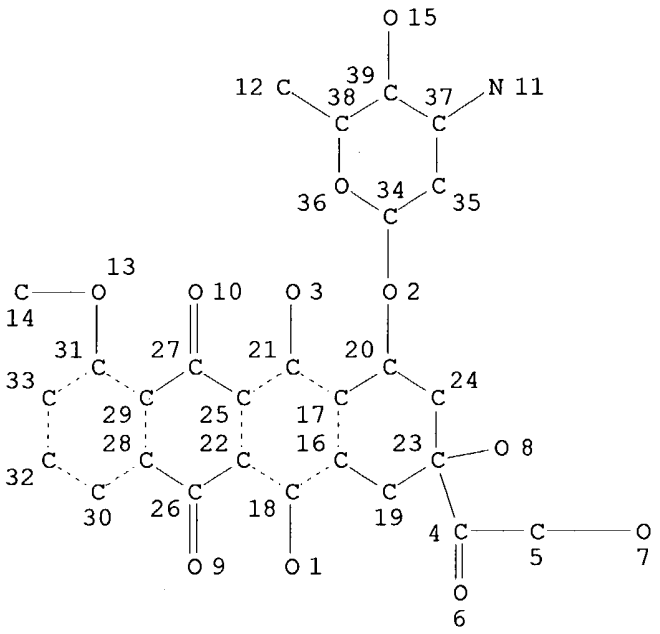


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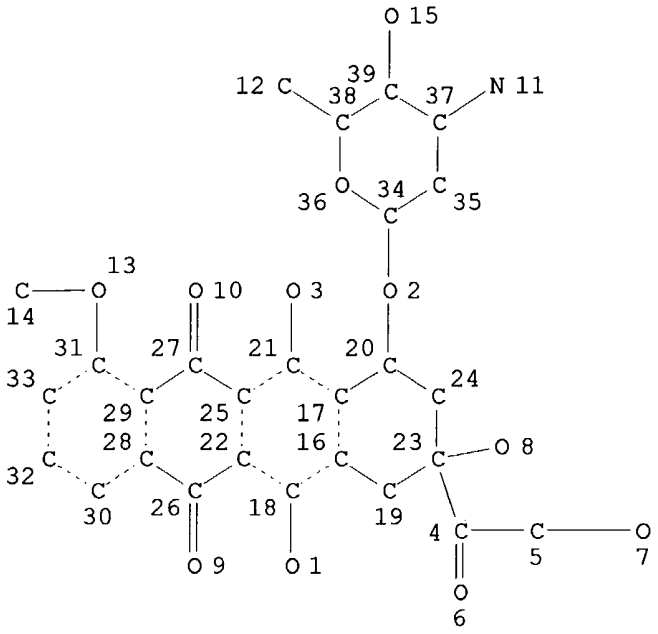

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L8            6 MITOXANTRONE

=> d rn

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RN   218350-47-1  REGISTRY


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218350-47-1 MAY NOT BE USED AS A MODEL
Structures which were created via the STRUCTURE command or are in the
Fragment File may be used as models in the STRUCTURE command.  Most,
but not all, substance Accession Numbers can also be used.
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OTHER NAMES:
CN   DNA (human S1-M1-80 cell clone MXR2 gene MXR2 mitoxantrone resistance
     protein 2 cDNA plus flanks)
CN   GenBank AF093772
FS   NUCLEIC ACID SEQUENCE
MF   Unspecified
CI   MAN
SR   GenBank
LC   STN Files:   CA, CAPLUS, GENBANK
DT.CA  CAplus document type:  Journal
RL.NP  Roles from non-patents:  BIOL (Biological study); PRP (Properties)
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 130:248466 CA
TI Molecular cloning of cDNAs which are highly overexpressed in mitoxantrone-resistant cells: Demonstration of homology to ABC transport genes
AU Miyake, Keisuke; Mickley, Lyn; Litman, Thomas; Zhan, Zhirong; Robey, Robert; Cristensen, Barbara; Brangi, Mariafiorella; Greenberger, Lee; Dean, Michael; Fojo, Tito; Bates, Susan E.
CS Medicine Branch National Cancer Institute, NIH, Bethesda, MD, 20892, USA
SO Cancer Research (1999), 59(1), 8-13
CODEN: CNREA8; ISSN: 0008-5472
PB AACR Subscription Office
DT Journal
LA English
AB Reports of multiple distinct mitoxantrone-resistant sublines without overexpression of P-glycoprotein or the multidrug-resistance associated protein have raised the possibility of the existence of another major transporter conferring drug resistance. In the present study, a cDNA library from mitoxantrone-resistant S1-M1-80 human colon carcinoma cells was screened by differential hybridization. Two cDNAs of different lengths were isolated and designated MXR1 and MXR2. Sequencing revealed a high degree of homol. for the cDNAs with Expressed Sequence Tag sequences previously identified as belonging to an ATP binding cassette transporter. Homol. to the Drosophila white gene and its homologues was found for the predicted amino acid sequence. Using either cDNA as a probe in a Northern anal. demonstrated high levels of expression in the S1-M1-80 cells and in the human breast cancer subline, MCF-7 AdVp3000. Levels were lower in earlier steps of selection, and in partial revertants. The gene is amplified 10-12-fold in the MCF-7 AdVp3000 cells, but not in the S1-M1-80 cells. These studies are consistent with the identification of a new ATP binding cassette transporter, which is overexpressed in mitoxantrone-resistant cells.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 218350-46-0 REGISTRY
CN DNA (human clone MXR1 transport protein ABC (ATP-binding cassette-containing) C-terminal fragment-specifying cDNA plus 3'-flank) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2378: PN: WO03038130 FIGURE: 3 claimed DNA
CN 3: PN: WO03008647 TABLE: 13b unclaimed DNA
CN **DNA (human S1-M1-80 cell clone MXR1 gene MXR1 mitoxantrone resistance protein 1 C-terminal fragment-specifying cDNA plus 3'-flank)**
CN GenBank AF093771
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PRP (Properties)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 138:380471 CA
TI Genes that are differentially expressed during erythropoiesis and their diagnostic and therapeutic uses
IN Brissette, William H.; Neote, Kuldeep S.; Zagouras, Panayiotis; Zenke, Martin; Lemke, Britt; Hacker, Christine
PA Pfizer Products Inc., USA; Max-Delbrueck-Centrum Fuer Molekulare Medizin
SO PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003038130	A2	20030508	WO 2002-US34888	20021031
	WO 2003038130	A3	20040212		
	WO 2003038130	C1	20040422		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2003038130	A2	20030508	WO 2002-XA34888	20021031
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004014064	A1	20040122	US 2002-285366	20021031
PRAI	US 2001-335048P	20011031			
	US 2001-335183P	20011102			
	WO 2002-US34888	20021031			

AB The present invention provides mol. targets that regulate erythropoiesis. Groups of genes or their encoded gene products comprise panels of the invention and may be used in therapeutic intervention, therapeutic agent screening, and in diagnostic methods for diseases and/or disorders of erythropoiesis. The panels were discovered using gene expression profiling of erythroid progenitors with Affymetrix HU6800 and HG-U95Av2 chips. Cells from an in vitro growth and differentiation system of SCF-Epo dependent human erythroid progenitors, E-cadherin+/CD36+ progenitors, cord blood, or CD34+ peripheral blood stem cells were analyzed. The HU6800 chip contains probes from 13,000 genes with a potential role in cell growth, proliferation, and differentiation and the HG-U95Av2 chip contains 12,000 full-length, functionally-characterized

genes. This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.

REFERENCE 2

AN 138:148639 CA
TI Comparison of protein or gene expression patterns of blood cells obtained by microarray to injury database to assess injury
IN Sharp, Frank R.; Tang, Yang; Lu, Aigang
PA University of Cincinnati, USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003008647	A2	20030130	WO 2001-US44278	20011128
	WO 2003008647	A3	20040325		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003104393	A1	20030605	US 2001-996275	20011128

PRAI US 2000-253568P 20001128
AB Methods of injury assessment in an individual include the steps of determining a pattern of expression exhibited by blood cells obtained from an individual and comparing the pattern of expression exhibited by the obtained blood cells to an injury database to assess the injury. The injury database includes genomic injury databases, proteomic injury databases, organ specific injury database, disease specific injury database. The patterns of gene or protein expression are obtained by microarray and analyzed by statistical anal., class prediction, clustering, and computer programs. The genes in the pattern of gene expression comprise acidosis-induced genes, hypoxia-induced genes, glucose-induced genes, ischemia-induced genes. The invention relates to sequences of two human genes which are expressed more highly in Parkinson's individuals. The invention also relates to genes associated with status epilepticus, hypoglycemia, ischemic stroke and hemorrhagic stroke in rat model. The invention also relates to gene expression pattern in males and females, resp. The invention also relates to assessing Parkinson's disease, stroke profusion, drug, neurofibromatosis, manic bipolar depression, migraine headache, schizophrenia, and Tourettes disease based on pattern of expression.

REFERENCE 3

AN 137:88421 CA
TI Genetic polymorphisms in genes associated with drug metabolism and their use in selecting drug therapies
IN Stanton, Vincent; Zillmann, Martin
PA USA
SO U.S. Pat. Appl. Publ., 210 pp., Cont.-in-part of U.S. Ser. No. 710,467.
CODEN: USXXCO
DT Patent
LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001034023	A1	20011025	US 2000-733000	20001207
	WO 2000050639	A2	20000831	WO 2000-US1392	20000120
	WO 2000050639	A3	20020510		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 2001034023	A1	20011025	US 2000-733000	20001207
PRAI	US 1999-131334P	19990426			
	US 1999-139440P	19990615			
	WO 2000-US1392	20000120			
	US 2000-696482	20001024			
	US 2000-710467	20001108			
	US 2000-733000	20001207			
	US 1999-121047P	19990222			
	US 1999-357743	19990720			

AB Methods for identifying and utilizing variances in genes relating to efficacy and safety of medical therapy and other aspects of medical therapy are described, including methods for selecting an effective treatment. [This abstract record is one of several records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

REFERENCE 4

AN 130:248466 CA

TI Molecular cloning of cDNAs which are highly overexpressed in mitoxantrone-resistant cells: Demonstration of homology to ABC transport genes

AU Miyake, Keisuke; Mickley, Lyn; Litman, Thomas; Zhan, Zhirong; Robey, Robert; Cristensen, Barbara; Brangi, Mariafiorella; Greenberger, Lee; Dean, Michael; Fojo, Tito; Bates, Susan E.

CS Medicine Branch National Cancer Institute, NIH, Bethesda, MD, 20892, USA

SO Cancer Research (1999), 59(1), 8-13
CODEN: CNREA8; ISSN: 0008-5472

PB AACR Subscription Office

DT Journal

LA English

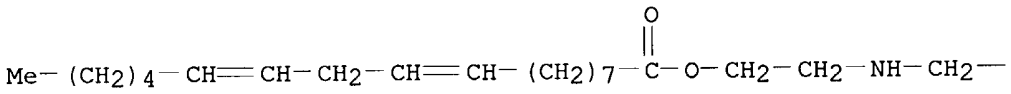
AB Reports of multiple distinct mitoxantrone-resistant sublines without overexpression of P-glycoprotein or the multidrug-resistance associated protein have raised the possibility of the existence of another major transporter conferring drug resistance. In the present study, a cDNA library from mitoxantrone-resistant S1-M1-80 human colon carcinoma cells was screened by differential hybridization. Two cDNAs of different lengths were isolated and designated MXR1 and MXR2. Sequencing revealed a high degree of homol. for the cDNAs with Expressed Sequence Tag sequences previously identified as belonging to an ATP binding cassette transporter. Homol. to the Drosophila white gene and its homologues was found for the predicted amino acid sequence. Using either cDNA as a probe in a Northern anal. demonstrated high levels of expression in the S1-M1-80 cells and in the human breast cancer subline, MCF-7 AdVp3000. Levels were lower in earlier steps of selection, and in partial revertants. The gene is amplified 10-12-fold in the MCF-7 AdVp3000 cells, but not in the S1-M1-80 cells. These studies are consistent with the identification of a new ATP

binding cassette transporter, which is overexpressed in mitoxantrone-resistant cells.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 158439-26-0 REGISTRY
CN 9,12-Octadecadienoic acid (9Z,12Z)-, 9,10-dihydro-5-hydroxy-9,10-dioxo-1,4-anthracenediylbis(imino-2,1-ethanediylimino-2,1-ethanediyl) ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9,12-Octadecadienoic acid (Z,Z)-, 9,10-dihydro-5-hydroxy-9,10-dioxo-1,4-anthracenediylbis(imino-2,1-ethanediylimino-2,1-ethanediyl) ester
OTHER NAMES:
CN **Mitoxantrone dilinoleate**
MF C58 H88 N4 O7
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PAGE 1-A



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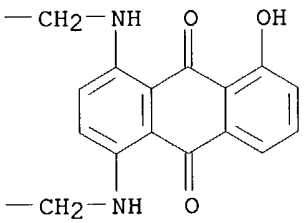


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

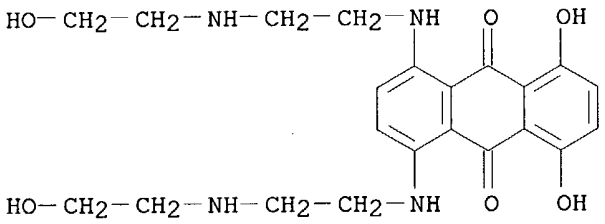
AN 121:238252 CA
TI Incorporation of lipophilic prodrugs of ametantrone and mitoxantrone inside low density lipoproteins (LDL) and selective uptake of the prodrug LDL complex via the LDL receptor pathway

AU Monard-Herkt, F.; Teissier-Morier, E.; Favre, G.; Samadi-Baboli, M.; Soula, G.; Houssin, R.; Bernier, J. L.; Henichart, J. P.; Martin-Nizard, F.; et al.
CS Pasteur Institute, Lille, Fr.
SO Acta Therapeutica (1993), 19(4), 317-35
CODEN: ACTTDZ; ISSN: 0378-0619
DT Journal
LA English
AB Low-d. lipoprotein (LDL) particles are potential drug carriers, but only lipophilic drug species partition into the core of the system. In this study, ametantrone (AQ) and mitoxantrone (DHAQ) have been coupled to different fatty acids (stearate, palmitate, oleate, linolenate). The linolenate esters of AQ and DHAQ incorporate in highest concentration into LDL using the following protocol of incubation. The prodrug (dilinolenate of DHAQ) was dissolved in Intralipid (a parental triglyceride rich emulsion) and then incubated with LDL and lipoprotein deficient serum or albumin for 18 h at 37°C. This method provides substantial incorporation of dilinolenate-DHAQ into LDL (26 mols. of dilinolenate-DHAQ per LDL particle). The dilinolenate-DHAQ-LDL complex was recognized by apolipoprotein B and E receptors, in vitro and in vivo in the rabbit. The pharmacol. efficiency of both free dilinolenate-DHAQ and dilinolenate-DHAQ-LDL complex was 1000 times less cytotoxic on A 549, A 431 and L 1210 cells than free DHAQ. We conclude that this method of incorporation allows the incorporation of a consistent concentration of prodrug inside LDL and prevents aggregation of the lipoprotein during the preparation of the prodrug-LDL complex. This complex is incorporated into the cell both in vitro and in vivo via the LDL receptor pathway.

L8 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 70711-41-0 REGISTRY
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]-, diacetate (salt) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Mitoxantrone diacetate**
CN NSC 299195
DR 137635-97-3
MF C22 H28 N4 O6 . 2 C2 H4 O2
LC STN Files: BIOSIS, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, RTECS*, TOXCENTER
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

CM 1

CRN 65271-80-9
CMF C22 H28 N4 O6



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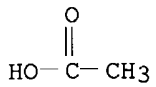
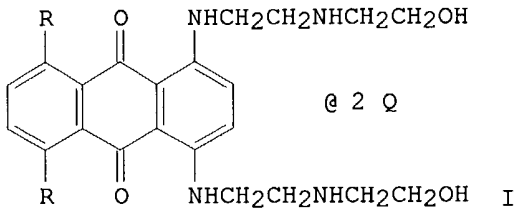
CRN 64-19-7
CMF C2 H4 O2



8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 119:116918 CA
TI Synthesis and characterization of anticancer anthraquinones: ametantrone and mitoxantrone
AU Chang, Pong
CS Sch. Pharm., Natl. Def. Med. Cent., Taipei, Taiwan
SO Proceedings of the National Science Council, Republic of China, Part A: Physical Science and Engineering (1992), 16(4), 304-10
CODEN: PNAEE2; ISSN: 0255-6588
DT Journal
LA English
GI



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AB Ametantrone (I, R = H, Q = AcOH) (3) and mitoxantrone I (R = OH, Q = HCl) are anthraquinone derivs. which possess potent cytotoxic activity against a variety of cancers in both animal and clin. studies. Ametantrone 3 was prepared by reacting leucoquinizarin 1 with 2-(2-aminoethylamino)ethanol, followed by air oxidation The corresponding leuco-compound, 2,3-dihydro-1,4,5,8-tetrahydroxy-9,10-anthracenedione 7, for the synthesis of mitoxantrone was not available. A synthetic route starting from chrysazin (4) was thus developed. Nitration of chrysazin 4, followed by reduction of the nitro- product gave 1,8-dihydroxy-4,5-diaminoanthraquinone (6), which on reductive hydrolysis yields 7. Then, by using the same procedures and reaction conditions as in the synthesis of ametantrone, mitoxantrone could be prepared with a total yield of 32%. Antileukemic activity of the synthesized mitoxantrone was conducted and proved to be equally potent by comparing with a com. product.

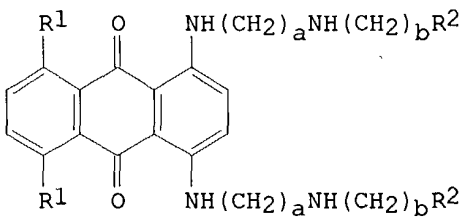
REFERENCE 2

AN 116:20794 CA
TI Preparation of 1,4-bis[(alkylamino)alkylamino]-9,10-anthracenediones
IN Zoelch, Lothar; Loeffler, Ralph; Kochmann, Werner; Holtz, Helmar; Schwabe, Konrad; Redslob, Joachim; Niclas, Hans Joachim; Heyer, Thomas; Buttke,

Klaus; et al.
PA Arzneimittelwerk Dresden G.m.b.H., Germany
SO Ger. (East), 6 pp.
CODEN: GEXXA8
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DD 290774	A7	19910613	DD 1988-312356	19880121
PRAI DD 1988-312356	19880121			

GI



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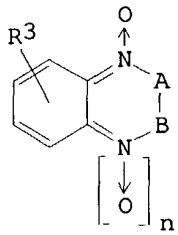


II

AB Title compds. I (R1,R2 = H, OH, NH2; a,b = 2-4; R1,R2, a,b can be the same or different) were prepared via oxidation of the corresponding 2,3-dihydro derivs. by 1-2 equivalent amine oxide II (R3 = H, Me, MeO, halo, NO2; AB = O, R4C:CR5; R4, R5 = H, Me; n = 0, 1; n = 0 when AB = O) at 10-30° in an organic solvent, e.g., ethylene glycol monomethyl ether optionally in the presence of an organic or inorg. acid. Thus, 5-methoxybenzofuroxan was added to a solution of 1,4-bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxy-2,3-dihydro-9,10-anthracenedione in MeOCH2OH at 0°. After 30 min at 0°, ethanolic HCl was added and the mixture was stirred 15 min further at 0°, ethanolic HCl was added and the mixture was stirred 15 min further at 0°, then warmed to 23°. The solution was stirred 20h at 23° to give the oxidized product in 91.1% yield.

REFERENCE 3

AN 113:184681 CA
TI Evidence for a common mechanism of action for antitumor and antibacterial agents that inhibit type II DNA topoisomerases
AU Huff, Anne C.; Kreuzer, Kenneth N.
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Journal of Biological Chemistry (1990), 265(33), 20496-505
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB Numerous antitumor and antibacterial agents inhibit type II DNA topoisomerases, yielding, in each case, a complex of enzyme covalently bound to cleaved DNA. The mechanism of inhibitor action was investigated by using the type II DNA topoisomerase of bacteriophage T4 as a model. The T4 topoisomerase is the target of antitumor agent 4'-(9-acridinylamino)methanesulfon-4-anisidide (m-AMSA) in T4-infected Escherichia coli. Two m-AMSA-resistant phage strains were previously isolated, one with a point mutation in topoisomerase subunit gene 39 and the other with a point mutation in topoisomerase subunit gene 52. The present study shows that the wild-type T4 topoisomerase is inhibited by six addnl. antitumor agents that also inhibit the mammalian type II topoisomerase: elipticine, 9-hydroxyellipticine, 2-methyl-9-hydroxyellipticinium acetate, mitoxantrone diacetate, teniposide, and

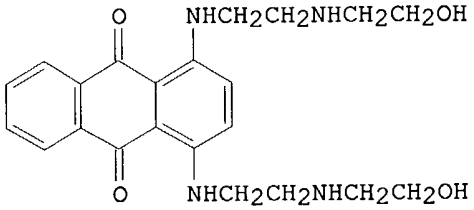
etoposide. Further, one or both of the m-AMSA-resistance mutations alters the enzyme sensitivity to each of these agents, conferring either cross-resistance or enhanced sensitivity. Finally, the gene 39 mutation confers on T4 topoisomerase a DNA gyrase-like sensitivity to the gyrase inhibitor oxolinic acid, thus establishing a direct link between the mechanism of action of the antibacterial quinolones and that of the antitumor agents. These results strongly suggest that diverse inhibitors of type II topoisomerases share a common binding site and a common mechanism of action, both of which are apparently conserved in the evolution of the type II DNA topoisomerases. Alterations in DNA cleavage site specificity caused by either the inhibitors or the m-AMSA-resistance mutations favor the proposal that the inhibitor binding site is composed of both protein and DNA.

REFERENCE 4

AN 111:70338 CA
TI Inhibitory effects of mitoxantrone and its analogs on a human hepatoma cell line in vitro
AU Liu, Tsung Yun; Yeh, Chang Huei; Chi, Chin Wen
CS Dep. Med. Res., Veterans Gen. Hosp., Taipei, Taiwan
SO Medical Science Research (1989), 17(12), 529-30
CODEN: MSCREJ; ISSN: 0269-8951
DT Journal
LA English
AB Among 4 anthracenediones tested, mitoxantrone (NSC 301739) was most potent against human hepatoma cells in vitro. Mitoxantrone, which is a HCl salt, was more active than the free base (NSC 279836), the diacetate (NSC 299195), and anthracenedione (NSC 196473). Mitoxantrone was cytotoxic compared to adriamycin in this system.

REFERENCE 5

AN 99:16204 CA
TI Comparative cytotoxicity of bisantrene, mitoxanthrone, ametantrone, dihydroxyanthracenedione, dihydroxyanthracenedione diacetate, and doxorubicin on human cells in vitro
AU Drewinko, Benjamin; Yang, Li Ying; Barlogie, Barthel; Trujillo, Jose M.
CS Dep. Lab. Med., Univ. Texas, Houston, TX, 77030, USA
SO Cancer Research (1983), 43(6), 2648-53
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
GI



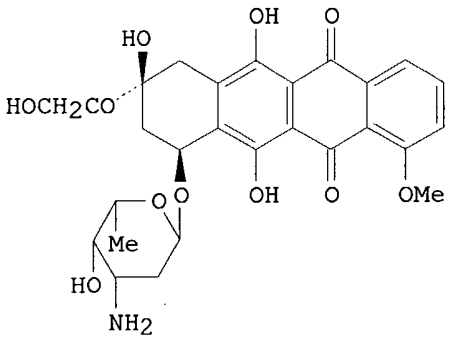
I

AB The cytotoxic efficacies of several substituted anthraquinones, ametantrone (I) [64862-96-0], dihydroxyanthracenedione [65271-80-9], dihydroxyanthracenedione diacetate [70711-41-0], mitoxanthrone [65271-80-9], bisantrene [78186-34-2], and doxorubicin, were evaluated on an established human colon adenocarcinoma cell line by the method of inhibition of colony formation. The concentration-dependent survival curve

following treatment for 1 h was biphasic and exponential for all agents. At concns. <1 μg/mL, mitoxanthrone was about twice as active as both hydroxyl-substituted anthracenediones and doxorubicin, .apprx.14 times more efficacious than I, and .apprx.22 times more powerful than bisantrene. At higher concns., these differences in efficacy became even more pronounced. Treatment in stationary phase decreased the lethal efficacy of doxorubicin but not that of the other agents. No recovery of potentially lethal or sublethal damage was noted for any agent, but for anthracenedione derivs., there was a small but statistically significant increase in cell kill during fractionated exposure. Continuous treatment with mitoxanthrone or bisantrene resulted in marked degrees of cell killing, reaching 99.95 and 99.5%, resp., after 24 h. For doxorubicin, cell kill efficacy declined after 4 h. Mitoxantrone was 10-fold more active on cells in G2 phase than on those in mid- to late-S phase. Sensitivity in G1 phase was immediate. Thus, mitoxanthrone appears as the most active compound while bisantrene and I are the least active agents. The cytotoxic efficacy of bisantrene increases during prolonged continuous exposure, while that of mitoxanthrone increases in fractionated administration. These characteristics could be exploited in clin. strategies designed to improve the performance of these agents.

REFERENCE 6

AN 96:97147 CA
TI Inhibition of cardiac guanylate cyclase by doxorubicin and some of its analogs: possible relationship to cardiotoxicity
AU Lehotay, Denis C.; Levey, Barbara A.; Rogerson, Brian J.; Levey, Gerald S.
CS Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA
SO Cancer Treatment Reports (1982), 66(2), 311-16
CODEN: CTRRDO; ISSN: 0361-5960
DT Journal
LA English
GI



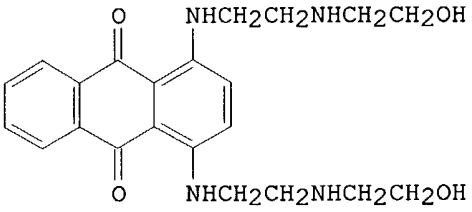
I

AB The effect of 30 analogs of doxorubicin (I) on cardiac guanylate cyclase [9054-75-5] activity. Structural modifications of these anthracycline antibiotics altered their effect on rat cardiac guanylate cyclase activity. N-Substitution on the sugar moiety eliminated the inhibitory action observed with the parent compound Long-chain hydrocarbon substitutions in place of the Me ketone side chain had a similar effect. Removal of substitution of the C-4 methoxy group had little or no effect on the ability of these compds. to modify guanylate cyclase activity. Substitutions of the C-9 side chain by a hydrazone derivative resulted in compds. that stimulated the enzyme. All of the anthracenedione derivs. were inhibitory. A comparison of the inhibitory effect of some of these anthracycline derivs. on in vitro cardiac guanylate cyclase activity with

their cardiotoxic potency suggests a possible relationship between these 2 parameters.

REFERENCE 7

AN 94:132036 CA
TI Comparative structure-genotoxicity study of three aminoanthraquinone drugs and doxorubicin
AU Au, William W.; Butler, Mary Ann; Matney, Thomas S.; Loo, Ti Li
CS Health Sci. Cent., Univ. Texas, Houston, TX, 77030, USA
SO Cancer Research (1981), 41(2), 376-9
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
GI



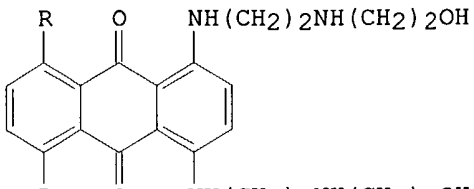
I

AB The genotoxic effects of 1,4-bis[2-[(2-hydroxyethyl)amino]ethylamino]-9,10-anthracenedione (HAQ) [64862-96-0] and 1,4-dihydroxy-5,8-bis[2-[(2-hydroxyethyl)amino]ethylamino]-9,10-anthracenedione (DHAQ)(I) [65271-80-9] and a new analog, 1,4-dihydroxy-5,8-bis[2-[(2-hydroxyethyl)amino]ethylamino]-9,10-anthracenedione diacetate (I diacetate) [70711-41-0], were analyzed by using mammalian cell cytogenetic assays (chromosome breakage and sister chromatid exchanges) as well as bacterial mutagenesis assays. The exptl. therapeutic activities of these drugs in vivo correlated well with their in vitro genetic toxicities as revealed by cytogenetic assays; i.e., the drug with the highest therapeutic activity (DHAQ) was most active in inducing chromosome damage. DHAQ was also more genotoxic than adriamycin [23214-92-8]. In cytogenetic assays, the activities of all drugs were reduced to different degrees in the presence of a S-9 metabolic system. Discrepancies were observed between results obtained from cytogenetic assays and those from mutagenesis assays. Whereas DHAQ was most active in cytogenetic studies, adriamycin was most mutagenic or toxic. HAQ was least active cytogenetically, and this activity was not changed appreciably in the presence of metabolic enzymes. However, it was metabolically activated to a bacterial mutagen. Apparently, the cytogenetic and mutagenesis assays may be sensitive to the activities of different agents and of different moieties of the same agent. The application of short-term in vitro assays to identify the chemical structures responsible for genetic toxicity and for therapeutic activities in vivo may lead to the better understanding of drug activities and to the development of more effective drugs.

REFERENCE 8

AN 91:32660 CA
TI Experimental antitumor activity of aminoanthraquinones
AU Johnson, Randall K.; Zee-Cheng, Robert K. Y.; Lee, William W.; Acton, Edward M.; Henry, David W.; Cheng, C. C.
CS Life Sci. Div., Arthur D. Little, Inc., Cambridge, MA, 02140, USA
SO Cancer Treatment Reports (1979), 63(3), 425-39
CODEN: CTRRDO; ISSN: 0361-5960

DT Journal
LA English
GI

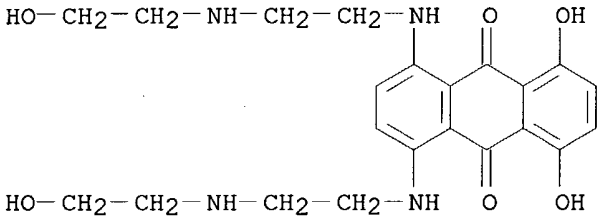


I, R=H
II, R=OH

AB The activity of a number of substituted alkylaminoanthraquinones was compared in transplanted murine tumor systems including P388 and L1210 leukemias, B16 melanoma, and colon carcinoma 26. Structure-activity relations among this class of compds. are discussed. Several derivs. had very high antitumor activity in several tumor systems. Two of the most active derivs., 1,4-bis{2-[(2-hydroxyethyl)amino]ethylamino}-9,10-anthracenedione (I) [64862-96-0] and 1,4-dihydroxy-5,8-bis{2-[(2-hydroxyethyl)amino]ethylamino}-9,10-anthracenedione (II) [65271-80-9], which had curative activity in the above-mentioned tumors, were compared in considerable detail. II showed distinct advantages over I in several tumor systems and was 10-fold more potent with respect to ED range. This last difference is important for 2 reasons. First, these aminoanthraquinones are strong and persistent blue dyes and the administration of lower doses would minimize a potential cosmetic drawback of these compds. Second and most important, i.v. administration of dose levels of I which are within the therapeutic dose range on intermittent dose schedules produced convulsions and immediate death. I.v. administration of II also caused acute toxicity, but, because of its increase potency relative to antitumor activity and delayed toxicity, this acute toxicity was apparent only at doses well above the therapeutic dose range. All of the aminoanthraquinones evaluated, regardless of their activity as antitumor agents in vivo, proved to be potent inhibitors of DNA and RNA synthesis in vitro and bound strongly to DNA as evidenced by ΔTm values (ΔTm = upward shift in DNA melting temperature). Thus, the strong antitumor activity of aminoanthraquinones would appear to be due to some mechanism other than, or in addition to, DNA binding and inhibition of nucleic acid synthesis.

L8 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 70476-82-3 REGISTRY
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Bisantrone
CN CL 232315
CN DHAD
CN Immunex
CN **Mitoxantrone dihydrochloride**
CN **Mitoxantrone hydrochloride**
CN Novantrone
CN Novatrone
CN NSC 301739
MF C22 H28 N4 O6 . 2 Cl H
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, HSDB*, IMSCOSEARCH, IMSPATENTS, IMSRESEARCH,

IPA, MRCK*, MSDS-OHS, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative)
CRN (65271-80-9)



●2 HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

172 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
172 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1

AN 140:332048 CA
TI Adjuvant cytotoxic and endocrine therapy in pre- and postmenopausal patients with breast cancer and one to nine infiltrated nodes. Five-year results of the Hellenic Cooperative Oncology Group randomized HE 10/92 study
AU Fountzilas, George; Stathopoulos, G.; Kouvatseas, G.; Polychronis, A.; Klouvas, G.; Samantas, E.; Zamboglou, N.; Kyriakou, K.; Adamou, A.; Pectasidis, D.; Ekonomopoulos, Th.; Kalofonos, H. P.; Bafaloukos, D.; Georgoulias, V.; Razis, E.; Koukouras, D.; Zombolas, V.; Kosmidis, P.; Skarlos, D.; Pavlidis, N.
CS AHEPA Hospital, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece
SO American Journal of Clinical Oncology (2004), 27(1), 57-67
CODEN: AJCODI; ISSN: 0277-3732
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The present randomized phase III trial was designed to detect a 15% benefit in relapse-free survival (RFS) or overall survival (OS) from the incorporation of adjuvant tamoxifen to the combination of CNF

[cyclophosphamide, 500 mg/m2; mitoxantrone (Novantrone), 10 mg/m2; fluorouracil, 500 mg/m2] chemotherapy and ovarian ablation in premenopausal patients with node-pos. breast cancer and conversely from the incorporation of CNF chemotherapy to adjuvant tamoxifen in node-pos. postmenopausal patients. From Apr. 1992 until Mar. 1998, 456 patients with operable breast cancer and one to nine infiltrated axillary nodes entered the study. Premenopausal patients were treated with six cycles of CNF chemotherapy followed by ovarian ablation with monthly injections of triptoreline 3.75 mg for 1 yr (Group A, 84 patients) or the same treatment followed by 5 yr of tamoxifen (Group B, 92 patients). Postmenopausal patients received 5 yr of tamoxifen (Group C, 145 patients) or 6 cycles of CNF followed by 5 yr of tamoxifen (Group D, 135 patients). Adjuvant radiation was administered to all patients with partial mastectomy. After a median follow-up period of 5 yr, 125 patients (27%) relapsed and 79 (17%) died. The 5-yr actuarial RFS for premenopausal patients was 65% in Group A and 68% in Group B ($p = 0.86$) and for postmenopausal patients 70% in Group C and 67% in Group D ($p = 0.36$). Also, the resp. OS rates were 77% and 80% ($p = 0.68$) for premenopausal and 84% and 78% ($p = 0.10$) for postmenopausal patients. Severe toxicities were infrequently seen, with the exception of leukopenia (18%), among the 311 patients treated with CNF. In conclusion, the present study failed to demonstrate a 15% difference in RFS in favor of node-pos. premenopausal patients treated with an addnl. 5 yr of tamoxifen after CNF adjuvant chemotherapy and ovarian ablation. Similarly, six cycles of CNF preceding 5 yr of tamoxifen did not translate to a 15% RFS benefit in node-pos. postmenopausal patients.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 2

AN 140:209872 CA

TI Improved liquid chromatographic method for mitoxantrone quantification in mouse plasma and tissues to study the pharmacokinetics of a liposome entrapped mitoxantrone formulation

AU Johnson, Jenifer L.; Ahmad, Ateeq; Khan, Sumsullah; Wang, Yue-Fen; Abu-Qare, Aqel W.; Ayoub, Jennifer E.; Zhang, Allen; Ahmad, Imran

CS Research and Development, Pharmacokinetics, Safety, and Efficacy Department, NeoPharm Inc., Waukegan, IL, 60085, USA

SO Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2004), 799(1), 149-155
CODEN: JCBAAI; ISSN: 1570-0232

PB Elsevier B.V.

DT Journal

LA English

AB A simple, rapid HPLC method for quantification of mitoxantrone in mouse plasma and tissue homogenates in the presence of a liposome entrapped mitoxantrone formulation (LEM-ETU) is described. Sample preparation is achieved by protein precipitation of 100 μl plasma or 200 μl tissue homogenate with an equal volume of methanol containing 0.5 M hydrochloric acid:acetonitrile (90:10, volume/volume). Ametantrone is used as the internal standard (i.s.). Mitoxantrone and i.s. are separated on a C18 reversed phase HPLC column, and quantified by their absorbance at 655 nm. In plasma, the standard curve is linear from 5 to 1000 ng/mL, and the precision (%CV) and accuracy (percentage of nominal concentration) are within 10%. In mouse tissue (heart, kidney, liver, lung, and spleen) homogenates (5%, w/v), the standard curve is linear from 25 to 2000 ng/mL, with acceptable precision and accuracy. The method was used to successfully quantify mitoxantrone in mouse plasma and tissue samples to support a pharmacokinetic study of LEM-ETU in mice.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 3

AN 140:156561 CA
TI Mitoxantrone (Novantrone) in multiple sclerosis: new insights
AU Neuhaus, Oliver; Kieseier, Bernd C.; Hartung, Hans-Peter
CS Department of Neurology, Heinrich Heine University, Duesseldorf, D 40225, Germany
SO Expert Review of Neurotherapeutics (2004), 4(1), 17-26
CODEN: ERNXAR; ISSN: 1473-7175
PB Future Drugs Ltd.
DT Journal; General Review
LA English
AB A review. The conclusions of a recent study of mitoxantrone (Novantrone) in multiple sclerosis and the approval of several health authorities support its use in patients with active relapsing-remitting or secondary progressive multiple sclerosis. This drug profile provides an outline on relevant preclin. and clin. studies, discusses relevant side effects of the compound and places mitoxantrone in the context of other therapeutic approaches available against this disabling disorder.
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 4

AN 140:122184 CA
TI Clinical effects of combination therapy with mitoxantrone, vincristine, and prednisolone in breast cancer
AU Katsumata, Kenji; Tomioka, Hidenori; Kusama, Mikihiro; Aoki, Tatsuya; Koyanagi, Yasuhisa
CS Department of Surgery, Tokyo Medical University, Shinjuku-ku, Tokyo, 160-0023, Japan
SO Cancer Chemotherapy and Pharmacology (2003), 52(1), 86-88
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal
LA English
AB Purpose. We assessed the clin. efficacy and safety of mitoxantrone hydrochloride which has been used as an anticancer drug in our hospital to treat breast cancer patients since 1993. Methods: A group of 23 patients with breast cancer were given one course of the following regimen every 3 wk: mitoxantrone hydrochloride (8 mg/m2 i.v. day 1), vincristine sulfate (1.2 mg/m2 i.v. day 1), and prednisolone (30 mg orally days 1-7). Results. The response rate was 52.2% including a complete response in four patients, and a partial response in eight patients. Adverse drug reactions included leukocytopenia (78.3%, 18/23 patients), alopecia (30.8%, 7/23), and peripheral neuropathy and generalized fatigue (26.1%, 6/23). In patients responding to the drug regimen, 50% survival was 29 mo, and in those not responding it was 12 mo. Conclusion: Combination treatment with mitoxantrone hydrochloride, vincristine sulfate and prednisolone is an effective treatment for breast cancer.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 5

AN 140:84337 CA
TI Field enhancement near the annealed nanostructured gold detected by optical spectroscopy with the probe biomolecules
AU Strekal, N.; Askirka, V.; Maskevich, S.; Sveklo, I.; Nabiev, I.
CS Grodno State University, Grodno, 230023, Belarus
SO Physics, Chemistry and Application of Nanostructures: Reviews and Short

Notes to Nanomeeting 2003, [International Conference], Minsk, Belarus, May 20-23, 2003 (2003), 171-174. Editor(s): Borisenko, Victor E.; Gaponenko, S. V.; Gurin, V. S. Publisher: World Scientific Publishing Co. Pte. Ltd., Singapore, Singapore.
CODEN: 69EJNT; ISBN: 981-238-381-6

DT Conference

LA English

AB Tailoring of spectral properties of vacuum deposited gold films with substrate annealing procedure allows to excite selectively the surface-enhanced Raman scattering (SERS) or the surface-enhanced fluorescence (SEF) of biomols. without changing a light source. The phenomenon can be explained in the context of self-assembling of gold granules on sprayed film and tuning up the position of localized plasmon (LP) excitation band to the mol. absorption. The separation of mols. from nanostructured gold surface on long distances results in further increasing of surface-enhanced secondary emission. The long-range field enhancement is discussed as collective effect of several interacting gold islands. The possible geometry of probe disposition in "hot spots" on self-aggregated gold films is presented.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 6

AN 140:64847 CA

TI Permeation of cytotoxic formulations through swatches from selected medical gloves

AU Klein, Michael; Lambov, Nikolai; Samev, Nikola; Carstens, Gerhard

CS St. Bernward-Apotheke, Hannover, Germany

SO American Journal of Health-System Pharmacy (2003), 60(10), 1006-1011
CODEN: AHSPEK; ISSN: 1079-2082

PB American Society of Health-System Pharmacists

DT Journal

LA English

AB The permeability of selected medical glove materials to various cytotoxic agents is described. Fifteen cytotoxic agents were prepared at the highest concns. normally encountered by hospital personnel. Four single-layer and two double-layer glove systems made of two materials-latex and neoprene-were exposed to the drugs for 30, 60, 90, 120, 150, and 180 min. Circular sections of the glove material were cut from the cuff and evaluated without any pretreatment. Permeability tests were conducted in an apparatus consisting of a donor chamber containing the cytotoxic solution and a collection chamber filled with water (the acceptor medium). The two sections were separated by the glove material. Permeating portions, collected in water as the acceptor medium, were analyzed by either UV-visible light spectrophotometry or high-performance liquid chromatog. (HPLC). Permeation rates were calculated on the basis of the concentration of the cytotoxic agent in the acceptor medium. Spectrophotometric measurements were taken every 30 min, and HPLC anal. was performed at the end of the three-hour period. Average permeation rates for 14 drugs were low (<0.2 nmol/[min · cm2]) or no permeation was detected in all glove materials. All glove materials tested were impermeable to most of the cytotoxic agents over a period of three hours. Carmustine was the only agent that substantially permeated single-layer latex glove materials. Permeation of most tested cytotoxic formulations was low through swatches of material from various medical gloves.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 7

AN 140:35511 CA
TI First-line intra-arterial chemotherapy (IAC) with epirubicin and mitoxantrone in locally advanced breast cancer
AU Fiorentini, G.; Tsetis, D.; Bernardeschi, P.; Varveris, C.; Rossi, S.; Kalogeraki, A.; Athanasakis, E.; Dentico, P.; Kanellos, P.; Biancalani, M.; Alamarashdah, S.; Zacharioudakis, G.; Saridaki, Z.; Chalkiadakis, G.; Xynos, E.; Zoras, O.
CS Department of Oncology and Hematology, "S. Giuseppe" City Hospital, Florence, Italy
SO Anticancer Research (2003), 23(5B), 4339-4345
CODEN: ANTRD4; ISSN: 0250-7005
PB International Institute of Anticancer Research
DT Journal
LA English
AB Approx. 20% of patients with breast cancer present with locally advanced disease without distant metastases. This phase II double-center trial aimed at investigating the activity of epirubicin (Farmorubicin) - mitoxantrone (Onkotrone/Novantrone) combination as first-line intra-arterial chemotherapy (IAC) in locally advanced breast cancer patients. Thirty-six patients with locally advanced disease and no prior exposure to anthracyclines received the following regimen: epirubicin (Farmorubicin) 30 mg/mq and mitoxantrone (Onkotrone/Novantrone) 10 mg/mq by IAC short infusion on day 1, every 3 wk for up to six cycles. Prior to IAC an arteriogram of subclavian, internal mammary and lateral thoracic arteries was obtained in all patients, followed by infusion of a blue dye solution into the arteries to determine the most appropriate vessel that supplies the tumor area. Objective responses, confirmed at least 4 wk after the first documentation, were observed in 25 patients (70%; 95%CI, 62% to 80%): 3 CR, 22 PR. Although three of the patients showed complete tumor regression, operative removal or toilet mastectomy became feasible in 25 patients since tumor shrinkage ranged over 75%. A total of 25 mastectomies were carried out for 36 patients. Four patients had bulky tumors (>13 cm tumor diameter), while 8 patients had ulcerated tumors, two of which presented with complete infiltration of normal breast tissue. The median time to progression and median overall survival were 11 and 27 mo, resp. The time to local response was 3 wk and time to mastectomy was 9 wk. Transient neurol. disorders developed in six patients and skin chemical burns with painful inflammatory reactions were encountered in ten patients. No systemic toxicity was observed in terms of bone marrow depression and hair loss. No cardiotoxicity was observed In all specimens necrosis was reported (complete 3 cases, partial 16 and minimal 6). A combination of epirubicin (Farmorubicin) and mitoxantrone (Onkotrone/Novantrone) as IAC appears to be a safe and well tolerated treatment for locally advanced breast cancer without clin. evidence of distant metastases. When combined with surgery it offers interesting results in terms of local control and allows a high rate of mastectomies in otherwise inoperable cases.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 8

AN 140:19910 CA
TI Pharmaceutical compositions for coating medical implants
IN Hunter, William L.; Gravett, David M.; Toleikis, Philip M.; Liggins, Richard T.; Loss, Troy A. E.
PA Angiotech Pharmaceuticals, Inc., Can.
SO PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003099346	A2	20031204	WO 2003-US16719	20030527
	WO 2003099346	A3	20040318		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2004043052	A1	20040304	US 2003-447309	20030527

PRAI US 2002-383419P 20020524

AB Medical implants are provided which release an anthracycline, fluoropyrimidine, folic acid antagonist, podophyllotoxin, camptothecin, hydroxyurea, and/or platinum complex, thereby inhibiting or reducing the incidence of infection associated with the implant. Thus, a solution was prepared by dissolving 100-mg 5-FU into 20-mL MeOH. A polyurethane catheter tubing was immersed in this solution for 16 h. The catheter tubing was vacuum dried at 50° for 16 h.

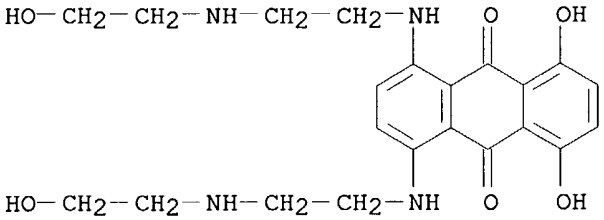
REFERENCE 9

AN 140:12588 CA
TI Reversal of multidrug resistance in mouse lymphoma cells by phenothiazines
AU Molnar, Joseph; Molnar, Annamaria; Mucsi, Ilona; Pinter, Oliver; Nagy, Beatrix; Varga, Andreas; Motohashi, Noboru
CS Department of Microbiology, Albert Szent-Gyorgyi Medical University, Szeged, Hung.
SO In Vivo (2003), 17(2), 145-150
CODEN: IVIVE4; ISSN: 0258-851X
PB International Institute of Anticancer Research
DT Journal
LA English
AB Various compds. were tested with regard to their reversal of multidrug resistance (MDR) in mouse tumor cells transfected with the human MDR1 gene. Phenothiazines containing aromatic moieties were bound through stacking interaction involving the polarization of the aromatic amino-acid substituents at the target site of p-glycoprotein (Pgp) 170, as a consequence of their large dipoles (as in the binding of phenothiazine to calmodulin-like structures). Acting as a calcium channel blocker, verapamil may induce conformational changes in the calcium channel-like structures of the transmembrane regions of Pgp. Most probably the tyrosine moieties of Pgp are involved in the action of verapamil and phenothiazines. Tomato lectin specifically binds to the polylactosamine moiety of Pgp170 at the first loop of Pgp. Other targets in the membrane may exist in close proximity to Pgp170, such as conA-reactive glycoproteins with terminal mannosyl residues. WGA-reactive N-acetyl glucosamine residues can also be modified resulting in conformational changes in transmembrane regions of the ABC transporter. The authors' results demonstrate that MDR can be reversed by interaction of various compds. with Pgp or by modification of the membrane structure around the Pgp.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 10

AN 140:619 CA
TI Cardiac adverse effects associated with mitoxantrone (Novantrone) therapy in patients with MS. [Erratum to document cited in CA138:379010]
AU Ghalie, R. G.; Edan, G.; Laurent, M.; Macuch, E.; Eisenman, S.; Hartung, H. P.; Gonsette, R. E.; Butine, M. D.; Goodkin, D. E.
CS Immunex Corp., Seattle, WA, USA
SO Neurology (2003), 60(1), 157
CODEN: NEURAI; ISSN: 0028-3878
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB There is an error in the dosage listed on page 910, under the Results section. The beginning of the second paragraph of the Results section should read as follows: "Phase 3 trial of MITO in MS (MIMS trial). Of the 124 patients who received MITO in the MIMS trial, 64 received 5 mg/m2 MITO and 60 received 12 mg/m2 MITO every 3rd month for up to 2 yr.".

L8 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2004 ACS on STN
RN 65271-80-9 REGISTRY
CN 9,10-Anthracenedione, 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,4-Bis[(2-(2-hydroxyethylamino)ethyl)amino]-5,8-dihydroxyanthraquinone
CN 1,4-Dihydroxy-5,8-bis-[[2-[(2-hydroxyethyl)amino]ethyl]amino]anthraquinone
CN 1,4-Dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]-9,10-anthracenedione
CN DHAQ
CN Dihydroxyanthraquinone
CN Mitoxanthrone
CN **Mitoxantrone**
CN Mitozantrone
CN Novantron
CN NSC 279836
FS 3D CONCORD
DR 137635-96-2, 70945-62-9
MF C22 H28 N4 O6
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2202 REFERENCES IN FILE CA (1907 TO DATE)
79 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2210 REFERENCES IN FILE CAPLUS (1907 TO DATE)

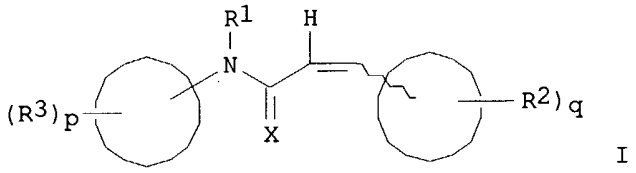
REFERENCE 1

AN 140:374987 CA
TI Preparation of aryl and heteroaryl propene amides as antiproliferative agents
IN Reddy, M. V. Ramana; Reddy, E. Premkumar
PA Temple University - of the Commonwealth System of Higher Education, USA
SO PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

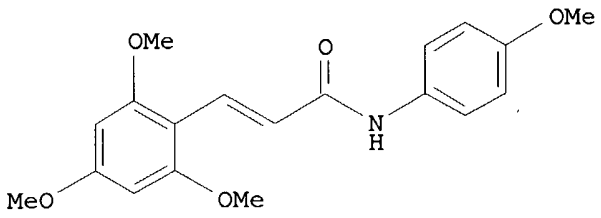
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004037751	A2	20040506	WO 2003-US26954	20030828

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-406766P 20020829
GI



I



II

AB Title compds. I [A, B = (hetero)aryl; X = O, S; R1 = sulfonylalkyl, acyl, carboxy, etc.; R2 = alkoxy, halo, CN, carboxy, carboxamido, etc.; R3 = halo, alkyl, alkoxy, CN, etc.; p = 1-3; q = 1-5] are prepared For instance, 4-methoxyphenylamino-3-oxopropanoic acid is reacted with 2,4,6-trimethoxybenzaldehyde to give II. Representative examples of activities of compds. I in cell lines (e.g., BT20, DU145) are reported. I are useful as antiproliferative agents, radioprotective agents and cytoprotective agents, including, for example, anticancer agents.

REFERENCE 2

AN 140:368313 CA
TI Dysregulation of protein kinase C activity in chemoresistant metastatic breast cancer cells
AU Schoendorf, Thomas; Hoopmann, Markus; Breidenbach, Martina; Rein, Daniel T.; Goehring, Uwe-Jochen; Becker, Martina; Mallmann, Peter; Kurbacher, Christian M.
CS Department of Natural Sciences, University of Applied Sciences, Rheinbach, Germany
SO Anti-Cancer Drugs (2004), 15(3), 265-268
CODEN: ANTDEV; ISSN: 0959-4973
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB This study was performed to evaluate the role of protein kinase C (PKC) activity in the development of chemoresistance in clin. breast cancer cells. To simulate the clin. situation, native tumor cells derived from 10 patients with advanced breast cancer were brought into short-term cultures, and treated with anthracyclines (doxorubicin, mitoxantrone), paclitaxel and combinations, resp. After 3 days of incubation, we determined total PKC activity relative to each control incubated with blank medium. Furthermore, we determined the chemoresistance against these drugs from each cell population sep. Relative PKC activity ranged from 14 to 249%; 64% (37 of 58) of the breast cancer cell suspensions were considered chemoresistant. There was a non-significant trend to a higher relative PKC activity in resistant cells compared to non-resistant cells ($p = 0.058$), regardless of the antineoplastic agent investigated. The individual variability in both PKC activity and chemoresistance pattern revealed that dysregulated PKC activity mediates resistance to antineoplastics. To achieve clin. value, evaluation of more data

concerning the PKC signal-transduction pathway is necessary. New protocols of cancer treatment will require this information to be successful.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 3

AN 140:368312 CA

TI Combination with liposome-entrapped, ends-modified raf antisense oligonucleotide (LErafAON) improves the anti-tumor efficacies of cisplatin, epirubicin, mitoxantrone, docetaxel and gemcitabine

AU Pei, Jin; Zhang, Chuanbo; Gokhale, Prafulla C.; Rahman, Aquilur; Dritschilo, Anatoly; Ahmad, Imran; Kasid, Usha N.

CS Department of Radiation Medicine, Lombardi Cancer Center, Georgetown University Medical Center, Washington, DC, USA

SO Anti-Cancer Drugs (2004), 15(3), 243-253
CODEN: ANTDEV; ISSN: 0959-4973

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Raf-1 protein serine/threonine kinase plays an important role in cell proliferation and cell survival. We have previously described a novel cationic liposome-entrapped formulation of raf antisense oligodeoxyribonucleotide (LErafAON) and its use as a radiosensitizer. The aim of this study was to examine the effect of combination of LErafAON and a chemotherapeutic agent on growth of human prostate (PC-3) and pancreatic tumor xenografts in athymic mice (Aspc-1 and Colo 357). In PC-3 tumor-bearing mice, administration of a combination of LErafAON (i.v., 25 mg/kg/dose, + 10/16) and cisplatin (i.v., 11.0 mg/kg/dose, + 3), epirubicin (EPI) (i.v., 9.0 mg/kg/dose, + 3) or mitoxantrone (MTO) (i.v., 2.5 mg/kg/dose, + 3) led to enhanced tumor growth inhibition as compared with single agents (LErafAON + cisplatin vs. cisplatin, $p < 0.0002$, $n = 8$; LErafAON + EPI vs. EPI, $p < 0.0001$, $n = 6$; LErafAON + MTO vs. MTO, $p < 0.05$, $n = 5$). In prostate or pancreatic tumor-bearing mice, combination of LErafAON (i.v., 25 mg/kg/dose, + 10/13) with docetaxel (Taxotere) (i.v., 5, 7.5 or 10 mg/kg/dose, + 2/4) led to tumor regression or enhanced growth inhibition as compared with single agents (PC-3: LErafAON + Taxotere vs. Taxotere, $p < 0.02$, $n = 7$; Aspc-1: LErafAON + Taxotere vs. Taxotere, $p < 0.03$, $n = 5$; Colo 357: LErafAON + Taxotere vs. Taxotere, $p < 0.04$, $n = 7$). Combination of LErafAON (i.v., 25 mg/kg/dose, + 10/13) with gemcitabine (i.v., 75 mg/kg/dose, + 4/6) also caused a significant tumor growth inhibition in the two pancreatic carcinoma models studied (Aspc-1: LErafAON + gemcitabine vs. gemcitabine, $p < 0.0001$, $n = 7$; Colo 357: LErafAON + gemcitabine vs. gemcitabine, $p < 0.002$, $n = 5$). LErafAON treatment (i.v., 25 mg/kg/dose, + 10) caused inhibition of Raf-1 protein expression in these tumor tissues (around 25-60%, $n = 4-7$). Interestingly, Taxotere treatment per se also led to decreased steady state level of Raf-1 protein in PC-3 and Aspc-1 tumor tissues (i.v., 10 mg/kg/dose, + 1 or 7.5 mg/kg/dose, + 2; around 25-80%, $n = 2/6$). Present studies demonstrate enhanced tumor growth inhibition or regression in response to a combination of a chemotherapeutic drug and LErafAON. These data provide a proof-of-principle for the clin. use of LErafAON in combination with chemotherapy for cancer treatment.

RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 4

AN 140:368289 CA

TI The cytoplasmic trafficking of DNA topoisomerase IIα correlates with

etoposide resistance in human myeloma cells
AU Engel, Roxane; Valkov, Nikola I.; Gump, Jana L.; Hazlehurst, Lori; Dalton, William S.; Sullivan, Daniel M.
CS H. Lee Moffitt Cancer Center and Research Institute, Departments of Interdisciplinary Oncology and Biochemistry and Molecular Biology, Experimental Therapeutics Program, University of South Florida, Tampa, FL, 33612, USA
SO Experimental Cell Research (2004), 295(2), 421-431
CODEN: ECREAL; ISSN: 0014-4827
PB Elsevier Science
DT Journal
LA English
AB In this study the authors have investigated the role of topoisomerase (topo) IIα trafficking in cellular drug resistance. To accomplish this, it was necessary to sep. the influence of cell cycle, drug uptake, topo protein levels, and enzyme trafficking on drug sensitivity. Thus, the authors developed a cell model (called accelerated plateau) using human myeloma H929 cells that reproducibly translocates topo IIα to the cytoplasm. Compared to log-phase cells, the cytoplasmic redistribution of topo IIα in plateau-phase cells correlated with a 10-fold resistance to VP-16 and a 40-60% reduction in the number of drug-induced double-strand DNA breaks. In addition, 7-fold more VP-16 was necessary to achieve 50% topo IIα band depletion, suggesting that there are fewer drug-induced topo-DNA complexes formed in quiescent cells than in log-phase cells. The total cellular amount of topo IIα and topo IIβ protein in log- and plateau-phase cells was similar as determined by Western blot anal. There was a 25% reduction in S-phase cell number in plateau cells (determined by bromodeoxyuridine (BrdU) incorporation), while there was no significant difference in the equilibrium concns. of [3H]-VP-16 when log cells were compared with plateau cells. Furthermore, the nuclear/cytoplasmic ratio of topo IIα is increased 58-fold in accelerated-plateau H929 cells treated with leptomycin B (LMB) when compared to untreated cells. It appears that the nuclear-cytoplasmic shuttling of topo IIα, which decreases the amount of nuclear target enzyme, is a major mechanism of drug resistance to topo II inhibitors in plateau-phase myeloma cells.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 5

AN 140:368210 CA
TI Highly Altered Protein Expression Profile in the Adriamycin Resistant MCF-7 Cell Line
AU Gehrmann, Marion L.; Fenselau, Catherine; Hathout, Yetrib
CS Department of Chemistry and Biochemistry, University of Maryland, College Park, MD, 20742, USA
SO Journal of Proteome Research (2004), 3(3), 403-409
CODEN: JPROBS; ISSN: 1535-3893
PB American Chemical Society
DT Journal
LA English
AB The protein expression pattern in the cytosol fraction of the adriamycin resistant MCF-7 cell line (MCF-7/ADR) was compared to that of the parental MCF-7 cell line using two-dimensional gel electrophoresis and mass spectrometry. Twenty proteins with altered abundances were identified and studied in MCF-7/ADR. Both up regulation and down regulation are characterized. The most striking differences were found for proteins that were uniquely expressed in this cell line and not detectable in the parental MCF-7 cell line. These proteins include annexin I, the neuronal ubiquitin carboxyl hydrolase isoenzyme L-1 (also known as PGP9.5),

glutathione-S-transferase pi class, nicotinamide N-methyltransferase, and interleukin-18 precursor. On the other hand, catechol-O-methyltransferase was expressed in the parental cell line, but was not detected in the adriamycin resistant cell line. This protein expression pattern was unique to MCF-7/ADR and not observed in MCF-7 cell lines selected for resistant to etoposide, mitoxantrone or melphalan.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 6

AN 140:362998 CA
TI Gamma irradiation of solid nanoparticulate active agents
IN Lee, Robert; Hilborn, Matthew; Kline, Laura; Keller, Janine
PA Elan Pharma International Limited, Ire.
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032980	A1	20040422	WO 2003-US27484	20030904

PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-415749P 20021004
AB The present invention relates to methods for terminal sterilization of solid forms of nanoparticulate active agent compns. via gamma irradiation The nanoparticulate active agent has an effective average particle size of less than about 2 μ, prior to incorporation into a solid form for sterilization. The resultant sterilized compns. exhibit excellent redispersibility, homogeneity, and uniformity. Also encompassed are compns. made via the described method and methods of treating animals and humans using such compns. Several examples are provided of γ-ray sterilization of naproxen nanoparticulate formulations. Pre-lyophilization, post-lyophilization and post-γ-irradiation properties (particle size, stability, osmolality, pH, microbiol. testing) are described. Surface stabilizers are used.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 7

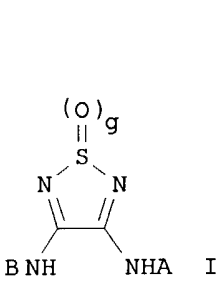
AN 140:357355 CA
TI Preparation of diaminothiadiazole dioxides and monoxides as CXC- and CC-chemokine receptor ligands
IN Taveras, Arthur G.; Chao, Jianhua; Biju, Purakkattle J.; Yu, Younong; Fine, Jay S.; Hipkin, William; Aki, Cynthia J.; Merritt, J. Robert; Li, Ge; Baldwin, John J.; Lai, Gaifa; Wu, Minglang; Hecker, Evan A.
PA Pharmacopeia, Inc., USA
SO PCT Int. Appl., 540 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

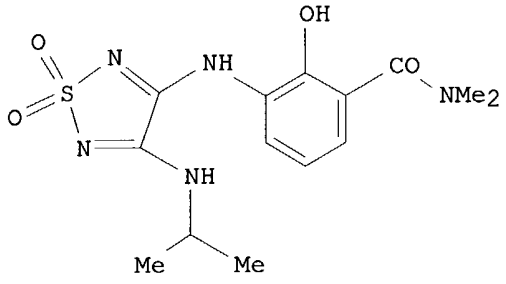
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033440	A1	20040422	WO 2003-US31707	20031007

PI WO 2004033440 A1 20040422 WO 2003-US31707 20031007
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NI, NO, NZ, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-417371P 20021009
GI



I



II

AB Disclosed are diaminothiadiazole mono- and dioxides (shown as I; e.g. II) and the pharmaceutically acceptable salts and solvates thereof. Examples of substituent A include heteroaryl, aryl, heterocycloalkyl, cycloalkyl, aryl, alkynyl, alkenyl, aminoalkyl, alkyl or amino; examples of substituent B include aryl and heteroaryl; g = 1, 2. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and cardiac reperfusion injury, acute pain, acute and chronic inflammatory pain, and neuropathic pain using I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 31% yield from the 4-methoxy analog and isopropylamine in the presence of DIEA in MeOH; the 4-methoxy analog was prepared from the dimethoxy analog and N,N-dimethyl-3-amino-2-hydroxybenzamide in 99% crude yield. Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 8

AN 140:350542 CA
TI Antitumor effects of imatinib (glivec, STI-571) to inhibit breast cancer resistance protein (BCRP)
IN Houghton, Peter J.; Traxler, Peter
PA Novartis Ag, Switz.; Novartis Pharma GmbH; St. Judes Children's Research Hospital
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent

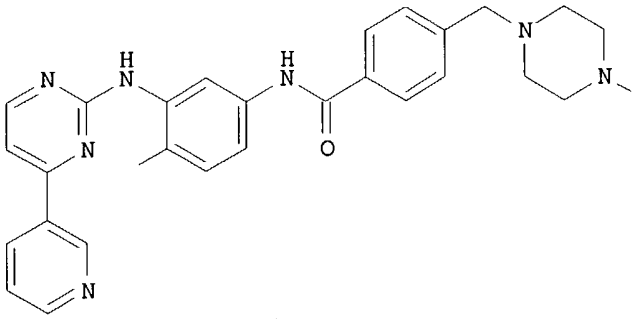
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004032925	A1	20040422	WO 2003-EP11271	20031010

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRAI US 2002-417915P 20021011
GI



I

AB The invention discloses the use of imatinib of the following formula (I) or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment of a cancer that expresses breast cancer resistant protein (BCRP) in a human subject in need of such a treatment. The invention further discloses to a method of treating cancers that demonstrate BCRP-mediated resistance to one or more therapeutic agents wherein imatinib is co-administered with the therapeutic agent.

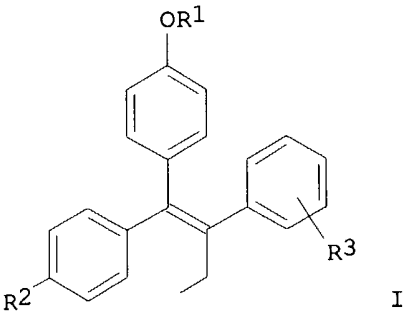
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE 9

AN 140:350535 CA
TI 1,1,2-Triphenyl-1-butene derivatives for overcoming antitumor drug resistance
IN Sugimoto, Yoshikazu; Tsukahara, Satomi; Sugimoto, Yoshikazu
PA Taiho Pharmaceutical Co., Ltd., Japan; National Cancer Center
SO Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2004123567	A2	20040422	JP 2002-286577	20020930

PRAI JP 2002-286577 20020930
GI



I

AB 1,1,2-Triphenyl-1-butene derivs. (I; R1 = H, -(CH2)n-NR4R5, -(CH)-SO2R4, with n = 1-4, R4, R5 = H, alkyl; R2 = OH, alkoxy, etc.) and their pharmaceutically acceptable salts are claimed for overcoming antitumor drug resistance from topoisomerase I and II inhibitors, including canptotecins e.g. irinotecan, topotecan, and SN-38.

REFERENCE 10

AN 140:350201 CA
TI ABCG2 overexpression in colon cancer cells resistant to SN38 and in irinotecan-treated metastases
AU Candeil, Laurent; Gourdier, Isabelle; Peyron, Delphine; Vezzio, Nadia; Copois, Virginie; Bibeau, Frederic; Orsetti, Beatrice; Scheffer, George L.; Ychou, Marc; Khan, Qasim A.; Pommier, Yves; Pau, Bernard; Martineau, Pierre; Del Rio, Maguy
CS CNRS-UMR 5160, Centre de Recherche en Cancerologie, CRLC Val d'Aurelle, Montpellier, 34298, Fr.
SO International Journal of Cancer (2004), 109(6), 848-854
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Overcoming drug resistance has become an important issue in cancer chemotherapy. Among all known mechanisms that confer resistance, active efflux of chemotherapeutic agents by proteins from the ATP-binding cassette family has been extensively reported. The aim of the present study was to determine the involvement of ABCG2 in resistance to SN38 (the active metabolite of irinotecan) in colorectal cancer. By progressive exposure to increasing concns. of SN38, we isolated 2 resistant clones from the human colon carcinoma cell line HCT116. These clones were 6- and 53-fold more resistant to SN38 than the HCT116-derived sensitive clone. Topoisomerase I expression was unchanged in our resistant variants. The highest resistance level correlated with an ABCG2 amplification. This overexpression was associated with a marked decrease in the intracellular accumulation of SN38. The inhibition of ABCG2 function by Ko143 demonstrated that enhanced drug efflux from resistant cells was mediated by the activity of ABCG2 protein and confirmed that ABCG2 is directly involved in acquired resistance to SN38. Furthermore, we show, for the first time in clin. samples, that the ABCG2 mRNA content in hepatic metastases is higher after an irinotecan-based chemotherapy than in irinotecan-naive metastases. In conclusion, this study supports the potential involvement of ABCG2 in the development of irinotecan resistance in vivo.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT